HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

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Original Article

Title

HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

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IRB: The study was approved by the institutional review board (IRB) of the National Center for AIDS/STD Control and Prevention of the China CDC.

Data sharing: Extra data is available by Dongliang Li, ldl66@126.com

Article Focus:

- In China, homosexual transmission has now become a major mode of HIV transmission. However, HIV incidence among Chinese MSM remains poorly understood.
- To date, findings from the sparse handful of Chinese MSM cohort studies have been limited by small sample sizes, short term follow-up, or heavy loss to follow-up.

Key Messages:

- The present cohort study was conducted to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up.
- This study provides empirical HIV seroincidence data relevant for HIV prevention and intervention planning strategies among MSM in China.

Strengths and Limitations:

- Evidence-based studies among Chinese MSM are urgently needed to provide scientific decisions for prevention and control of HIV transmission.

Abstract

Objectives: 1) To assess the HIV incidence rate among men who have sex with men (MSM) in a large cohort study in Beijing, China; 2) To identify sociodemographic and behavioral risk factors of HIV seroconversion among MSM in Beijing, China.

Design: A prospective cohort study.

Setting: Baseline and follow-up visits were conducted among MSM in Beijing, China.

Participants: A cohort of 797 HIV-seronegative MSM was recruited from August to December 2009, with follow-up occurring after 6 and 12 months.

Primary and secondary outcome measures: At baseline and follow-up visits, participants reported sociodemographic and sexual behavior information, and were tested for HIV, HSV-2, and syphilis with whole blood specimens. Cox regression analysis was used to identify factors associated with HIV seroconversion.

Results: Most study participants (86.8%) were retained by the 12-month follow-up. The HIV, HSV-2 and syphilis incidence rates were 8.09 (95%CI: 6.92 to 9.26), 5.92 (95%CI: 5.44 to 6.40) and 8.06 (95%CI: 7.56 to 8.56) cases per 100 person-years, respectively. HIV seroconversion was significantly associated with being ≤25 years old, having < 12 years of education, having >1 male sex partner in the past 6 months, and being syphilis positive or HSV-2 positive.

Conclusions: The HIV incidence among MSM in Beijing is serious. Interventions and treatment of sexually transmitted diseases (STD) should be combined with HIV control and prevention measures among MSM.

Key Words: HIV; HSV-2; syphilis; men who have sex with men; cohort

BACKGROUND

It is estimated that 780,000 persons were living with HIV/AIDS (PLWHA) in China by the end of 2011, and that homosexual transmission is accounting for a greater proportion of HIV infections. Men who have sex with men (MSM) as a proportion of PLWHA in China rose from 7.3% in 2005, to 11.0% in 2007, and 17.4% in 2011[1]. Of China's 48,000 new HIV infections in 2011, 29.4% were attributed to homosexual transmission[1]. The HIV epidemic in China is still on the rise, and homosexual transmission has become a major mode of transmission.

Although many cross-sectional studies have reported on HIV prevalence among MSM in China, data on HIV incidence rates among this sub-population remains limited. Among the only three MSM cohort studies which have been conducted to date in China, HIV incidence rates ranged between 2.6 and 5.4 cases per 100 person-years[2–4]. Unfortunately, two of these studies were characterized by small sample sizes, short term follow-up, or heavy loss to follow-up. The most recent cohort study was only able to recruit 218 eligible MSM participants, 44% of whom were lost to follow-up[4]. In response, the present cohort study was designed to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up. In order to better guide HIV prevention and intervention programs among MSM in China, this study focuses on two key objectives: 1) Assess the HIV, HSV-2 and syphilis incidence rates among MSM in Beijing, China; and 2) Identify

sociodemographic and behavioral risk factors of HIV seroconversion among MSM in Beijing, China.

METHODS

Study design and participant recruitment

This prospective cohort study was conducted in Beijing, the capital of China. Participants were recruited using three methods. First, study participants were recruited directly through website advertisements by a non-governmental AIDS volunteer group (www.hivolunt.net). Second, peer recruiters were hired and trained to distribute flyers with study related information at MSM-frequented venues (e.g., MSM clubs, bars, parks and bathhouses). Third, study participants were encouraged to refer their peers to attend this study. Prospective study participants then came to a Beijing study clinic that was easily accessible via various transportation routes. Baseline participant inclusion criteria included ≥18 years old, male, had anal or oral sex with another man in the past 6 months, and provided written informed consent with their actual name or nickname. Baseline participant exclusion criteria were HIV-seropositive status, lack of contact information, and planned relocation away from Beijing within the next year. A total of 962 participants were screened during administration of the baseline survey from August to December 2009, of whom 61 were HIV positive, 36 could not provide contact information, 56 planned to relocate away from Beijing within the next year, and 12 refused to participate in follow-up

visits; thus, a total of 797 eligible participants were enrolled into the cohort study, each of whom was assigned a unique and confidential study identification code.

Study participants were followed-up for one year, with follow-up visits occurring at 6 and 12 months. At each study visit (i.e., baseline, 6-month follow-up, and 12-month follow-up), trained health professionals conducted one-on-one questionnaire-based interviews with eligible participants in a private room of the study clinic. After interviews were completed, confidential HIV voluntary counseling and testing (VCT) was conducted, followed by a clinical STD examination by experienced physicians. Venipuncture blood samples were collected from each participant and tested for HIV, syphilis and HSV-2. To ensure confidentiality, each participant was required to provide their pre-assigned identification code in order to receive their test results, which became available after one week. All participants who tested positive for HSV-2 and syphilis were referred to an STD clinic or hospital for appropriate treatment. After each completed study visit, participants received 50 RMB (approximately $7.40 USD), 12 free condoms and one free lubricant. At completion of the baseline and 6-month follow-up visits, each participant was asked to return for a follow-up evaluation after 6 months. The study was approved by the Institutional Review Boards of the National Center for AIDS/STD Control and Prevention of the China Center for Disease Control and Prevention.

Questionnaire measures

Sociodemographic measures included participant age, ethnicity, education, marital status, Beijing permanent residency status, income, and housing status. Behavioral measures included self-identified sexual orientation, sought male sex partners on the internet, sought male sex partners in bathhouse/public washroom/park, had HIV tested in the past year, participated in HIV intervention program in the past year, number of MSM social contacts, number of male sex partners in the past 6 months, had commercial sex (i.e., bought or sold sex) with male partners in the past 6 months, had unprotected anal sex with regular or casual male partners in the past 6 months, had sex with female partners in the past 6 months, had STD syndrome in the past 6 months, bought condom/lubricant in the past 6 months, and used illicit drugs in past 6 months.

Laboratory tests

Blood samples were tested for HIV, HSV-2 and syphilis infections. The HIV infection status was determined with an enzyme-linked immunosorbent assay (ELISA) (InTec Products Company, China) screening and an HIV-1/2 Western Blot confirmation (HIV Blot 2.2 WBTM, Genelabs Diagnostics). HSV-2 infection status was determined using ELISA (Trinity Laboratories, USA). Syphilis infection status was determined with a rapid plasma reagin (RPR) test (Shanghai Rongsheng, China) and

confirmation of positive tests by the Treponema pallidum particle assay (TPPA) test (Fujirebio inc., Japan).

Statistical analysis

Questionnaire-based data and biological testing results were recorded, double checked and compared with EpiData software (EpiData 3.0 for windows; The EpiData Association, Odense, Denmark). After corrections, data were then converted and analyzed using statistical analysis system (SAS 9.1 for windows; SAS Institute Inc, Cary, NC). To identify correlates of time to HIV seroconversion, the Cox regression model was used in univariate and multiple regression analyses. Statistically significant variables in univariate analyses were then entered simultaneously into a multiple Cox regression model. The assumed time of seroconversion was the half-way time point between the participant's last negative HIV test and first positive HIV test. Statistical significance was defined as *P*-value <0.05 (two-tailed).

Results

Baseline characters of the participants

Of the 797 participants, 448 were recruited by peer referral, 173 were recruited by the internet, and 158 were recruited by outreach. The median age was 28 years; 92.6%

belonged to the Han ethnic group; and 51.9% graduated from high school or above. Beijing permanent residents accounted for 18.7%; the median monthly income was US $294; 61.7% were single, 17.7% were married, and 15.7% were cohabiting with male or female sex partners; 67.6% identified as homosexual, and 32.4% identified as heterosexual or bisexual. The median age of sexual debut was 20 years old and the median age of homosexual sexual debut was 25 years old; 65.8% and 34.2% experienced their sexual debut with another male and female, respectively.

Regarding behaviors in the past 6 months among study participants, the median number of male sex partners was 2; 6.0% bought or sold sex with male sex partners; 23.7% had unprotected anal sex with regular male sex partners; 12.9% had unprotected anal sex with casual male sex partners; 17.7% had sex with female sex partners; 11.8% had unprotected sex with female sex partners; and 1.0% used illicit drugs. Experience of an STD syndrome in the past year was reported by 17.2% of participants. Prevalence of syphilis and HSV-2 was 16.4% and 4.6%, respectively. Descriptive results are shown in Table 1.

Cohort retention and contact information

Of the 797 participants, 96.5% (769/797) were retained in the cohort at the 6-month follow-up, and 86.8% (692/797) were retained at the 12-month follow-up. Participants

were contacted for their 6 and 12 month follow-up visits by cell phone calls (1792), short text messages (2179) and QQ© (Tencent Inc. Beijing, China) or MSN© online social networking software (1369) (Web Messenger, Microsoft Cooperation, USA) (Table 2). Of the 692 participants retained in the cohort at the 12 month, 393 were followed up by cell phone calls, 121 by short text messages, 136 by QQ/MSN social networking software, and 29 by peer contacts.

Incidence of HIV, syphilis and HSV-2 and factors predicting HIV seroconversion

48 HIV seroconversions were observed over 592.98 person-years of observation, resulting in an incidence rate of 8.09 cases per 100 person-years (95%CI: 6.92 to 9.26). 30 syphilis seroconversions were observed over 506.06 person-years of observation, resulting in an incidence rate of 5.92 cases per 100 person-years (95%CI: 5.44 to 6.40). 46 HSV-2 seroconversions were observed over 570.61 person-years of observation, resulting in an incidence rate of 8.06 per 100 person-years (95%CI: 7.56 to 8.56).

Univariate and multivariate Cox regression analyses indicated that younger age, less education, having multiple male sex partners in the past 6 months, syphilis infection and HSV-2 infection were significantly associated with time to HIV seroconversion

(table 3). Results of the univariate and multivariate Cox regression analyses are shown in Table 3.

Discussion

The first objective of this large cohort study was to assess the HIV incidence rate among MSM in Beijing, China. Results indicate that the HIV incidence rate among MSM has increased dramatically. Previous cross-sectional studies in Beijing using the BED capture immunoassay (BED-CEIA) estimated the incidence of HIV was 2.9% in 2005 and 3.6% in 2006[5]. Previous prospective cohort studies conducted among MSM in Beijing found that the incidence rate increased from 2.6 cases per 100 person-years in 2007 to 3.4 cases per 100 person-years in 2008[2,6]. However, our large cohort study conducted from 2009-2010 shows that the HIV incidence rate among Beijing MSM has now increased to 8.09 cases per 100 person-years, an extremely high rate compared with other cities in both China and around the world[2–4,7–9]. HIV prevalence is also growing. Previous cross-sectional studies conducted among MSM in Beijing showed increasing HIV prevalence among this population, from 0.4% in 2004, 4.6% in 2005, to 5.8% in 2006[10], and 6.3% in 2009. The high HIV incidence rate and prevalence among MSM in Beijing indicate that the epidemic in this group is extremely serious and that effective intervention services are urgently needed.

Due to prevailing social stigma against MSM and MSM-associated behaviors in China and worldwide, conventional recruitment and cohort follow-up approaches with MSM remains challenging. Using multiple methods of recruitment and follow-up contact, this cohort study of 797 HIV-seronegative MSM was able to retain 86.8% of all participants after 12 months. This is the first large cohort study in China to evaluate the retention rate for a prospective cohort of MSM. Based on previous cohort studies among injection drug users and MSM [11–15], the following protocols were implemented in order to ensure greater participant retention at follow-ups: 1. an explicit cohort retention plan was written and adhered to throughout the study; 2. peer MSM staff were hired to contact participants; 3. all participants were asked to provide at least two different contact sources; and 4. participants had the flexibility of choosing cell phone calls, short text messages, and/or QQ/MSN internet social networking platforms as means by which study staff contacted them.

Many epidemiological studies have found a strong association between HSV-2 and syphilis infection and HIV infection among men, women and MSM, including longitudinal studies where HSV-2 infection preceded the HIV infection[16]. In this study, we found HSV-2 incidence was high among MSM and that HSV-2 infection also increased the risk of HIV acquisition. It was reported that persistence of HIV-1 receptor-positive cells after HSV-2 reactivation is a potential mechanism for increased

HIV-1 acquisition[17]. However, HSV-2 based HIV intervention studies continue to be disappointing, and the mechanisms of association between HSV-2 and HIV infection requires further study[18].

International studies have shown that younger MSM are at higher risk of HIV infection[9,19,20], minor geographic variations notwithstanding. Results from this study are consistent with such studies, and may be partly explained by China's changing social norms concerning homosexuality, brought about by the rapid economic and social development of the past thirty years. In traditional culture in China, MSM were severely socially marginalized and stigmatized. Virtually all MSM faced strong social pressure to hide their sexual orientation, and most of them eventually married. Today, China's social environment is gradually becoming less stigmatizing for MSM, whereby younger MSM are more active in homosexuality than older MSM. Older MSM are also more likely to be married. Furthermore, our previous study conducted in the same area showed that younger MSM were more likely to use the internet for sex seeking than older MSM[21], implying that younger MSM were likelier to have more casual sex partners and face higher risk. Meanwhile, these study results also imply that intervention and prevention should be focused on MSM with lower education and multiple male sex partners.

This study indicates that the HIV epidemic among MSM in Beijing is more serious than previously expected. Given the synergistic relationship between STD and HIV infection, interventions for high risk behaviors and treatment and management for STDs should be combined with HIV control and prevention initiatives among MSM in China. In short, evidence indicates that the HIV epidemic among MSM in Beijing is rapidly intensifying. Comprehensive actions are urgently needed and the time is now.

Our study has several limitations. Study subjects were recruited using non-random sampling methods that could have led to selection bias. Although the cohort retention was high, HIV, HSV-2, and syphilis incidence rates may have been significantly different among those lost to follow-up. These may have led to overestimation or underestimation of the true incidence. However, our baseline analyses indicated that demographic and behavioral characteristics were similar between those lost to follow-up and those retained in the cohort. We believe that these data will help future research towards innovative STD/HIV interventions for MSM in China, and mobilize government, public health and non-governmental communities to control the rapid transmission of HIV and STDs among Chinese MSM.

AUTHOR'S CONTRIBUTIONS

Dongliang Li, Shuming Li and Yingjie Liu: study design and data collection, manuscript writing.

Yanjie Gao, Mingrun Yu, Xueying Yang, Qingchun Li, Shulin Jiang, Zhenhai Zhou, Zheng Zhang, Li Yan, Guiyan Jiang, Dong Xiao: study design, data collection and manuscript writing

Stephen W. Pan, Yuhua Ruan, Fengji Luo, Yiming Shao: study design, data collection, data interpretation and manuscript writing.

Qingchun Li and Yuhua Ruan: data analysis.

Fengji Luo, Yiming Shao: PI.

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Table 1. Baseline characteristics of study participants

Factors	N	%
Overall	797	100
Age (median, years)	28	
Ethnicity		
Han	738	92.6
Minority	59	7.4
Education		
Less than high school	383	48.1
High school and above	414	51.9
Beijing permanent resident	149	18.7
Monthly income (median, US $)	294	
Marital status in the past 3 months		
Single	492	61.7
Married	141	17.7
Cohabiting with male or female sex partner	125	15.7
Separated or divorced or widowed	39	4.9
Sexual orientation		
Homosexual	539	67.6
Heterosexual or bisexual	258	32.4
Age of sexual debut (median, years)	20	
Age of homosexual debut (median, years)	25	
Partner of sexual debut		
Male	524	65.8
Female	273	34.2

Number of male sex partners in the past 6 months (median)	2	
Bought or sold sex with male sex partners in the past 6 months	48	6.0
Had unprotected anal sex with regular male sex partners in the past 6 month	189	23.7
Had unprotected anal sex with casual male partners in the past 6 month	103	12.9
Had sex with female sex partners in the past 6 months	141	17.7
Had unprotected sex with female sex partners in the past 6 month	94	11.8
Used illicit drugs in the past 6 months	8	1.0
Had STD syndrome in the past year	137	17.2
Syphilis positive	131	16.4
HSV-2 positive	37	4.6

Table 2. Contact patterns and times for cohort follow-up study

Follow-up	Cell phone call	Short text message	QQ/MSN	Peer contact	Email	Landline Telephone	Total
6-month	884	1075	665	87	31	5	2747
12-month	908	1104	704	93	43	2	2854
Total (%)	1792(32.0)	2179(38.9)	1369(24.4)	180(3.2)	74(1.3)	7(0.1)	5601(100.0)

Table 3. Factors associated with HIV seroconversions in a 12-month follow-up study among MSM

Factors	No. of seroconversions	Person-years	Incidence rate (per 100 person years)	HR (95% CI)	*P* value	*Adjusted* HR (95% CI)	*P* value
Total	48	592.98	8.09				
Age (years)							
>25	24	389.31	6.16	1.00		1.00	
≤25	24	203.67	11.78	1.96 (1.11, 3.45)	0.0198	2.59(1.41,4.75)	0.0021
Ethnicity							
Minorities	2	43.32	4.62	1.00			
Han	46	549.66	8.37	1.79 (0.44, 7.39)	0.4191		
Years of education							
>12	16	317.66	5.04	1.00		1.00	
≤12	32	275.31	11.62	2.68(1.43,5.02)	0.0021	2.12(1.12,4.03)	0.0213
Married/cohabiting with female sex partner							
No	36	401.14	8.97	1.00			
Yes	12	191.84	6.26	0.70 (0.36, 1.34)	0.2822		
Beijing permanent resident							
No	41	481.63	8.51	1.00			
Yes	7	111.34	6.29	0.74 (0.33, 1.64)	0.4542		
Monthly income (US $)							
≤440	32	388.45	8.24	1.00			
>440	16	204.52	7.82	0.94 (0.52, 1.71)	0.8365		
Sexual orientation							
Heterosexual/bisexual	10	194.52		1.00			
Homosexual	38	398.45	9.54	1.84 (0.92, 3.69)	0.0871		

Sought male sex partners on the internet							
No	19	255.49	7.44	1.00			
Yes	29	337.48	8.59	1.16 (0.65, 2.06)	0.6227		
Sought male sex partners in bathhouse/public washroom/park							
No	32	442.51	7.23	1.00			
Yes	16	150.46	10.63	1.48 (0.81, 2.70)	0.1994		
Had HIV test in the past year							
No	23	269.11	8.55	1.00			
Yes	25	323.87	7.72	0.89 (0.50, 1.56)	0.6789		
Participated in an HIV intervention program in the past year							
No	7	92.43	7.57	1.00			
Yes	41	500.55	8.19	1.08 (0.48, 2.40)	0.8555		
Number of MSM social contacts							
≤10	30	348.52	8.61	1.00			
>10	18	244.46	7.36	0.86 (0.48, 1.54)	0.6056		
Number of male sex partners in P6 M							
≤1	9	218.23	4.12	1.00		1.00	
>1	39	374.75	10.41	2.54 (1.23, 5.24)	0.0117	2.52(1.20,5.32)	0.015
Had unprotected anal sex with male in P6 M							
No	30	361.94	8.29	1.00			
Yes	18	231.04	7.79	0.94 (0.52, 1.69)	0.8469		
Had commercial sex with male in P6 M							
No	46	569.25	8.08	1.00			
Yes	2	23.73	8.43	1.06 (0.26, 4.38)	0.9314		
Had female sex partners in P6 M							

No	40	481.90	8.30	1.00			
Yes	8	111.08	7.20	0.87 (0.41, 1.86)	0.7249		
Had unprotected sex with female partners in P6 M							
No	43	520.92	8.25	1.00			
Yes	5	72.06	6.94	0.84 (0.33, 2.13)	0.7152		
Had STD syndrome in P6 M							
No	38	512.54	7.41	1.00			
Yes	10	80.43	12.43	1.69 (0.84, 3.40)	0.1388		
Bought condom/lubricant in P6 M							
No	26	321.90	8.08	1.00			
Yes	22	271.08	8.12	1.00 (0.57, 1.77)	0.9891		
Syphilis positive							
No	34	502.95	6.76	1.00		1.00	
Yes	14	90.02	15.55	2.35(1.26, 4.38)	0.0072	2.28(1.19,4.34)	0.0126
HSV-2 positive							
No	39	533.50	7.31	1.00		1.00	
Yes	9	59.48	15.13	2.07 (1.00, 4.27)	0.0497	4.01(1.61,9.97)	0.0029

P6M: the past 6 months.

Prof. Jackie Cassell Dr Stefan Baral
Editor in Chief Associate Editor
Sexually Transmitted Infections

Ref.: sextrans-2012-050665
HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

Dear Prof. Jackie Cassell and Dr Stefan Baral

Many thanks for the revision opportunity. Following your guidance, all of the issues and concerns raised were addressed point-by-point. ***We agree to transfer the manuscript to BMJ Open.***

Reviewer: 1
Comments to the Author
HIV incidence and risk factors for HIV infection in MSM in Beijing, China.

This is an interesting paper with valuable information about the rapid spread of HIV infection among MSM (or whatever men were enrolled in this study) in Beijing, China. The authors need to be congratulated with establishing such a high follow-up rate, which is unique for China, where cohort studies among MSM are a new research phenomenon and have been conducted only fairly recently.
The HIV incidence is the only reportable finding from this study and there is little doubt that in this group of men it is extremely high. However, we don't know to what extent these men represent the community at large, so we can't really generalize the number, except to the men in the study itself. If anything, we can say that in some groups of MSM, such as this one, the HIV incidence is very high. This is important to get out into the literature and to the HIV and MSM research community at large.
The risk factor analysis however, is not ready to be reported and should be shelved for a while until the authors have more thoroughly defined their population, variables, and type of statistical analysis, as well as applied different and more thorough approaches of statistical analysis. The reason is the identification of the size of the foreskin as a (modest) risk factor for HIV acquisition (while receptive anal sex was not). This implicates that HIV is transmitted through insertive (anal) sex more frequently and more efficiently than generally believed and documented in 30 years of risk factor analysis for prevalent and incident HIV infection in MSM. If this is true, this will need to be confirmed by many other studies and go through several rounds of scientific evaluations and community discussions as it is opposite to what is generally believed and has been very well established. However, I think there are too many uncertainties and too many unknowns in this paper to draw any conclusion in this

respect. I believe that if the variables and data are properly defined and statistically analyzed this finding will not hold up. First of all, only 67% of men identified as homosexual and only 46% reports anal intercourse (p. 11). This raises questions about whether we are looking at the right population of MSM or not and whether this is a group to study these types of factors. The foreskin variable is very poorly defined and there is no information about why it was assessed, how it was assessed, whether also was looked at width or only at length of the foreskin, the length of the foreskin proportionally to penis size both in flaccid and erect shape, and when a foreskin was considered too long. Was the effect of a too short or too narrow foreskin also evaluated? Where any rectal attributes assessed (narrow vs. wide anus, cq. sphincter?). Now we are there, I am just asking, because this would be the next logical step, a taboo thing to do, but likely having an effect. Since we are in physical attributes and approaching eugenics we need to reflect and ask ourselves what we are doing and if we really want to go there based on very poorly defined and assessed variables.

In the paper I'd like to see the proportions and interactions between receptive and insertive anal intercourse and foreskin variables as well as the incidence curves, proportionality and the like. Currently the reader has no information about this and cannot evaluate whether the conclusions of the authors are justified, or just confounded or collinear or whatever is the case.

The paper needs to be reviewed by an experienced biostatistician and edited by a scientific medical writer whose mother tongue is English and who both have knowledge of the international literature in this area.

Response:

Participants were recruited using three methods. First, study participants were recruited directly through website advertisements by a non-governmental AIDS volunteer group (www.hivolunt.net). Second, peer recruiters were hired and trained to distribute flyers with study related information at MSM-frequented venues (e.g., MSM clubs, bars, parks and bathhouses). Third, study participants were encouraged to refer their peers to attend this study.

We added on page 10 (results section): *Of the 797 participants, 448 were recruited by peer referral, 173 were recruited by the internet, and 158 were recruited by outreach.*

We have revised the Questionnaire measures on page 9: *Sociodemographic measures included participant age, ethnicity, education, marital status, Beijing permanent residency status, income, and housing status. Behavioral measures included self-identified sexual orientation, sought male sex partners on the internet, sought male sex partners in bathhouse/public washroom/park, had HIV tested in the past year, participated in HIV intervention program in the past year, number of MSM social contacts, number of male sex partners in the past 6 months, had commercial*

sex (i.e., bought or sold sex) with male partners in the past 6 months , had unprotected anal sex with regular or casual male partners in the past 6 months, had sex with female partners in the past 6 months, had STD syndrome in the past 6 months, bought condom/lubricant in the past 6 months, and used illicit drugs in past 6 months.

Due to the challenges of assessing foreskin size and the differential risks associated with insertive and receptive anal sex, among other confounding factors, we have removed the foreskin variable from the analyses and deleted Table 4. The results and discussion sections have been revised accordingly.

The paper has been reviewed and edited by an experienced biostatistician and a scientific medical writer whose mother tongue is English, both of whom are knowledgeable about the international literature in this area.

Reviewer: 2

This ms reports on HIV incidence and predictors of seroconversion among MSM in Beijing, China. The study recruited a large cohort of study participants and had a high retention rate. In general, the ms is well written and organized. However, several issues are of serious concern.

1. The argument for circumcision to reduce HIV incidence among MSM is on shaky ground based on the flawed analysis and measurement. First of all, what is "too long" of a foreskin? How was it defined? There does not seem to have any scientific and biological basis to suggest that longer foreskin increase HIV acquisition risk. The exposure is not through the foreskin rather the soft non-keratinized penis head. And the conclusion that "MSM who had foreskin is too long should clean their male penis in good hygiene…" (p.15) makes little sense. Second, if there is any protective effect, circumcision would only reduce HIV acquisition risk among those who engage in predominantly insertive AND unprotected anal sex. Although the sub-analysis (Table 4) excluded bottoms, it did not exclude those who practiced both insertive and receptive anal sex. Furthermore, it did not exclude those who practice safe sex all the time. The more appropriate analysis should be restricted to those who were uncircumcised, predominantly insertive, and engaged in unprotected anal sex at least sometimes. And how were the anal sex role measured?

Response:

Due to the challenges of assessing foreskin size and the differential risks associated with insertive and receptive anal sex, among other confounding factors, we have removed the foreskin variable from the analyses and deleted Table 4. The results and discussion sections have been revised accordingly.

2. The authors stated that previous cohorts of Chinese MSM were limited by sample

sizes and had low retention rates. This study compensated these limitations. What were the best strategies used to retain participants? What were the lessons learned? The authors should elaborate on these key points in the discussion section. The data presented in Table 2 is rather un-informative. Instead, what a reader would most like to know is which methods were more successful in retaining participants. Any perhaps certain methods were more effective in retaining certain sub-groups of MSM than others?

Response:

Regarding strategies used to retain participants, the following text was added to page 14:

> *"Based on previous cohort studies among injection drug users and MSM [11–15], the following protocols were implemented in order to ensure greater participant retention at follow-ups: 1. an explicit cohort retention plan was written and adhered to throughout the study; 2. peer MSM staff were hired to contact participants; 3. all participants were asked to provide at least two different contact sources; and 4. participants had the flexibility of choosing cell phone calls, short text messages, and/or QQ/MSN internet social networking platforms as means by which study staff contacted them."*

On page 12, we also added data regarding how successfully retained participants were contacted throughout the study:

> *"Of the 692 participants retained in the cohort at the 12 month, 393 were followed up by cell phone calls, 121 by short text messages, 136 by QQ/MSN social networking software, and 29 by peer contacts."*

3. There are many variables presented in the tables, especially Table 3, which were not described in the measures section. And some described in the results section were not in the tables. The authors should carefully double-check everything. The authors should also include unprotected receptive anal sex and unprotected insertive anal sex in the analysis, rather than just "unprotected anal sex in p6m."

Response:

The measures section, results section, and tables have been double-checked and are now consistent. Receptive or insertive anal intercourse was not asked of participants. Therefore, only "anal sex" is reported.

4. How were the participants who tested positive for HSV and syphilis at baseline handled? Did they receive appropriate treatment for the infections?

Response:

Yes, all participants who tested positive for HSV and/or syphilis at baseline were referred for appropriate treatment. The following text was added to page 8: (Study design and participant recruitment):

> *"All participants who tested positive for HSV-2 and syphilis were referred to an STD clinic or hospital for appropriate treatment."*

We hope these changes satisfactorily address the reviewers' comments and questions.

Thank you very much!

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HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

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Original Article

Title

HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

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Running Head

HIV incidence among MSM in China

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Conflicts of Interest: No.

IRB: The study was approved by the institutional review board (IRB) of the National Center for AIDS/STD Control and Prevention of the China CDC.

Data sharing: Supplementary data is available by contacting Dongliang Li, ldl66@126.com

Article Focus:

- In China, homosexual transmission has now become a major mode of HIV transmission. However, HIV incidence among Chinese MSM remains poorly understood.
- To date, findings from the sparse handful of Chinese MSM cohort studies have been limited by small sample sizes, short term follow-up, or heavy loss to follow-up.

Key Messages:

- The present cohort study was conducted to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up.
- This study provides empirical HIV seroincidence data relevant for HIV prevention and intervention planning strategies among MSM in China.

Strengths and Limitations:

- Evidence-based studies among Chinese MSM are urgently needed to provide scientific decisions for prevention and control of HIV transmission.

Abstract

Objectives: 1) To assess the HIV incidence rate among men who have sex with men (MSM) in a large cohort study in Beijing, China; 2) To identify sociodemographic and behavioral risk factors of HIV seroconversion among MSM in Beijing, China.

Design: A prospective cohort study.

Setting: Baseline and follow-up visits were conducted among MSM in Beijing, China.

Participants: A cohort of 797 HIV-seronegative MSM was recruited from August to December 2009, with follow-up occurring after 6 and 12 months.

Primary and secondary outcome measures: At baseline and follow-up visits, participants reported sociodemographic and sexual behavior information, and were tested for HIV, HSV-2, and syphilis with whole blood specimens. Cox regression analysis was used to identify factors associated with HIV seroconversion.

Results: Most study participants (86.8%) were retained by the 12-month follow-up. The HIV, HSV-2 and syphilis incidence rates were 8.09 (95%CI: 6.92 to 9.26), 5.92 (95%CI: 5.44 to 6.40) and 8.06 (95%CI: 7.56 to 8.56) cases per 100 person-years, respectively. HIV seroconversion was significantly associated with being ≤25 years old, having < 12 years of education, having >1 male sex partner in the past 6 months, and being syphilis positive or HSV-2 positive.

Conclusions: The HIV incidence among MSM in Beijing is serious. Interventions and treatment of sexually transmitted diseases (STD) should be combined with HIV control and prevention measures among MSM.

Key Words: HIV; HSV-2; syphilis; men who have sex with men; cohort

BACKGROUND

It is estimated that 780,000 persons were living with HIV/AIDS (PLWHA) in China by the end of 2011, and that homosexual transmission is accounting for a greater proportion of HIV infections. Men who have sex with men (MSM) as a proportion of PLWHA in China rose from 7.3% in 2005, to 11.0% in 2007, and 17.4% in 2011[1]. Of China's 48,000 new HIV infections in 2011, 29.4% were attributed to homosexual transmission[1]. Hence, the HIV epidemic in China is still on the rise and spreading among MSM.

Although many cross-sectional studies have reported on HIV prevalence among MSM in China, data on HIV incidence rates among this sub-population remain limited. Among the only three MSM cohort studies which have been conducted thus far in China, HIV incidence rates ranged between 2.6 and 5.4 cases per 100 person-years[2–4]. Unfortunately, two of these studies were characterized by small sample sizes, short term follow-up, or heavy loss to follow-up. The most recent cohort study was only able to recruit 218 eligible MSM participants, 44% of whom were lost to follow-up[4]. In response, the present cohort study was designed to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up. In order to better guide HIV prevention and intervention programs among MSM in China, this study focuses on two key objectives: 1) Assess the HIV, HSV-2 and syphilis incidence rates among MSM in Beijing, China; and 2) Identify

sociodemographic and behavioral risk factors of HIV seroconversion among MSM in Beijing, China.

METHODS

Study design and participant recruitment

This prospective cohort study was conducted in Beijing, the capital of China. Participants were recruited using three methods. First, study participants were recruited directly through website advertisements by a non-governmental AIDS volunteer group (www.hivolunt.net). Second, peer recruiters were hired and trained to distribute flyers with study related information at MSM-frequented venues (e.g., MSM clubs, bars, parks and bathhouses). Third, study participants were encouraged to refer their peers to enroll in the study. Prospective study participants then came to a Beijing study clinic that was easily accessible via various transportation routes. Baseline participant inclusion criteria included ≥18 years old, male, had anal or oral sex with another male in the past 6 months, and provided written informed consent with their actual name or nickname. Baseline participant exclusion criteria were HIV-seropositive status, lack of contact information, and planned relocation away from Beijing within the next year. A total of 962 participants were screened during administration of the baseline survey from August to December 2009, of whom 61 were HIV positive, 36 could not provide contact information, 56 planned to relocate away from Beijing within the next year, and 12 refused to participate in follow-up

visits; thus, a total of 797 eligible participants were enrolled into the cohort study, each of whom was assigned a unique and confidential study identification code.

Study participants were followed-up for one year, with follow-up visits occurring at 6 and 12 months. At each study visit (i.e., baseline, 6-month follow-up, and 12-month follow-up), trained health professionals conducted one-on-one questionnaire-based interviews with eligible participants in a private room of the study clinic. After interviews were completed, confidential HIV voluntary counseling and testing (VCT) was conducted, followed by a clinical STD examination by experienced physicians. Venipuncture blood samples were collected from each participant and tested for HIV, syphilis and HSV-2. To ensure confidentiality, each participant was required to provide their pre-assigned identification code in order to receive their test results, which became available after one week. All participants who tested positive for HSV-2 and syphilis were referred to an STD clinic or hospital for appropriate treatment. After each completed study visit, participants received 50 RMB (approximately $7.40 USD), 12 free condoms and one free lubricant. At completion of the baseline and 6-month follow-up visits, each participant was asked to return for a follow-up evaluation after 6 months. The study was approved by the Institutional Review Boards of the National Center for AIDS/STD Control and Prevention of the China Center for Disease Control and Prevention.

Questionnaire measures

Sociodemographic measures included participant age, ethnicity, education, marital status, Beijing permanent residency status, income, and housing status. Behavioral measures included self-identified sexual orientation, sought male sex partners on the internet, sought male sex partners in bathhouse/public washroom/park, had HIV tested in the past year, participated in HIV intervention program in the past year, number of MSM social contacts, number of male sex partners in the past 6 months, had commercial sex (i.e., bought or sold sex) with male partners in the past 6 months, had unprotected anal sex with regular or casual male partners in the past 6 months, had sex with female partners in the past 6 months, had STD syndrome in the past 6 months, bought condom/lubricant in the past 6 months, and used illicit drugs in past 6 months.

Laboratory tests

Blood samples were tested for HIV, HSV-2 and syphilis infections. The HIV infection status was determined with an enzyme-linked immunosorbent assay (ELISA) (InTec Products Company, China) screening and an HIV-1/2 Western Blot confirmation (HIV Blot 2.2 WBTM, Genelabs Diagnostics). HSV-2 infection status was determined using ELISA (Trinity Laboratories, USA). Syphilis infection status was determined with a rapid plasma reagin (RPR) test (Shanghai Rongsheng, China) and

confirmation of positive tests by the Treponema pallidum particle assay (TPPA) test (Fujirebio inc., Japan).

Statistical analysis

Questionnaire-based data and biological testing results were recorded, double checked and compared with EpiData software (EpiData 3.0 for windows; The EpiData Association, Odense, Denmark). After corrections, data were then converted and analyzed using statistical analysis system (SAS 9.1 for windows; SAS Institute Inc, Cary, NC). To identify correlates of time to HIV seroconversion, the Cox regression model was used in univariate and multiple regression analyses. Statistically significant variables in univariate analyses were then entered simultaneously into a multiple Cox regression model. The assumed time of seroconversion was the half-way time point between the participant's last negative HIV test and first positive HIV test. Statistical significance was defined as *P*-value <0.05 (two-tailed).

Results

Baseline characters of the participants

Of the 797 participants, 448 were recruited by peer referral, 173 were recruited by the internet, and 158 were recruited by outreach. The median age was 28 years; 92.6%

belonged to the Han ethnic group; and 51.9% graduated from high school or above. Beijing permanent residents accounted for 18.7%; the median monthly income was US $294; 61.7% were single, 17.7% were married, and 15.7% were cohabiting with male or female sex partners; 67.6% identified as homosexual, and 32.4% identified as heterosexual or bisexual. The median age of sexual debut was 20 years old and the median age of homosexual sexual debut was 25 years old; 65.8% and 34.2% experienced their sexual debut with another male and female, respectively.

Regarding behaviors in the past 6 months among study participants, the median number of male sex partners was 2; 6.0% bought or sold sex with male sex partners; 23.7% had unprotected anal sex with regular male sex partners; 12.9% had unprotected anal sex with casual male sex partners; 17.7% had sex with female sex partners; 11.8% had unprotected sex with female sex partners; and 1.0% used illicit drugs. Experience of an STD syndrome in the past year was reported by 17.2% of participants. Baseline prevalence of syphilis and HSV-2 was 16.4% and 4.6%, respectively. Descriptive results are shown in Table 1.

Cohort retention and contact information

Of the 797 participants, 96.5% (769/797) were retained in the cohort at the 6-month follow-up, and 86.8% (692/797) were retained at the 12-month follow-up. Participants

were contacted for their 6 and 12 month follow-up visits by cell phone calls (1792), short text messages (2179) and QQ© (Tencent Inc. Beijing, China) or MSN© online social networking software (1369) (Web Messenger, Microsoft Cooperation, USA) (Table 2). Of the 692 participants retained in the cohort at the 12 month, 393 were followed up by cell phone calls, 121 by short text messages, 136 by QQ/MSN social networking software, and 29 by peer contacts. There was no difference of sexual behaviors among subjects by method of follow-up.

Incidence of HIV, syphilis and HSV-2 and factors predicting HIV seroconversion

Among the 797 participants who were seronegative for HIV at baseline, 48 HIV seroconversions were observed over 592.98 person-years of observation, resulting in an incidence rate of 8.09 cases per 100 person-years (95%CI: 6.92 to 9.26). Among the 666 participants who were seronegative for syphilis at baseline, 30 syphilis seroconversions were observed over 506.06 person-years of observation, resulting in an incidence rate of 5.92 cases per 100 person-years (95%CI: 5.44 to 6.40). Among the 760 participants who were seronegative for HSV-2 at baseline, 46 HSV-2 seroconversions were observed over 570.61 person-years of observation, resulting in an incidence rate of 8.06 per 100 person-years (95%CI: 7.56 to 8.56).

Univariate and multivariate Cox regression analyses indicated that younger age, less education, having multiple male sex partners in the past 6 months, syphilis infection and HSV-2 infection were significantly associated with time to HIV seroconversion (table 3). Results of the univariate and multivariate Cox regression analyses are shown in Table 3.

Discussion

The first objective of this large cohort study was to assess the HIV incidence rate among MSM in Beijing, China. Results indicate that the HIV incidence rate among MSM has increased dramatically. Using the BED capture immunoassay (BED-CEIA), previous cross-sectional studies among MSM in Beijing have estimated HIV incidence at 2.9% in 2005 and 3.6% in 2006[5]. (Essentially, the BED assay calculates anti-HIV IgG relative to total IgG and is based on the principle that the ratio of anti-HIV IgG to total IgG increases with time shortly after HIV infection. This method enables cross-sectional serosurveys to estimate HIV-1 incidence and distinguish recent infections from long-term infections.) Previous prospective cohort studies conducted among MSM in Beijing found that the incidence rate increased from 2.6 cases per 100 person-years in 2007 to 3.4 cases per 100 person-years in 2008[2,6]. However, our large cohort study conducted from 2009-2010 shows that the HIV incidence rate among Beijing MSM has now increased to 8.09 cases per 100 person-years, an extremely high rate compared with other cities in both China and

around the world[2–4,7–9]. Explanations for the exceptionally high and steady rise in HIV incidence among Beijing MSM are not entirely clear, but one possibility may be that Beijing's relatively vibrant MSM culture facilitates greater dissasortative sexual mixing between MSM groups, which in turn can increase HIV background prevalence. Previous cross-sectional studies conducted among MSM in Beijing showed increasing HIV prevalence among this population, from 0.4% in 2004, 4.6% in 2005, to 5.8% in 2006[10], and 6.3% in 2009. The high HIV incidence rate and prevalence among MSM in Beijing indicate that the epidemic in this group is extremely serious and that effective intervention services are urgently needed.

Due to prevailing social stigma against MSM and MSM-associated behaviors in China and worldwide, conventional recruitment and cohort follow-up approaches with MSM remains challenging. Using multiple methods of recruitment and follow-up contact, we were able to retain 86.8% of all 797 participants after 12 months. This is the first large cohort study in China to evaluate the retention rate for a prospective cohort of MSM. Based on previous cohort studies among injection drug users and MSM [11–15], the following protocols were implemented in order to ensure greater participant retention: 1. An explicit cohort retention plan was written and adhered to throughout the study; 2. Peer MSM staff were hired to contact participants; 3. All participants were asked to provide at least two different means of contact; and 4. Participants had the flexibility of choosing cell phone calls, short text messages,

and/or QQ/MSN internet social networking platforms as the means by which study staff contacted them.

Many epidemiological studies have found that HIV infection is strongly associated with HSV-2 and syphilis [16]. In this study, we found that HSV-2 incidence was high among MSM and that HSV-2 infection also increased the risk of HIV acquisition. It has been reported that persistence of HIV-1 receptor-positive cells after HSV-2 reactivation is a potential mechanism for increased risk of HIV-1 acquisition[17]. However, HSV-2 based HIV intervention studies continue to be disappointing, and the mechanisms of association between HSV-2 and HIV infection requires further study[18].

International studies have shown that younger MSM are at higher risk of HIV infection[9,19,20], minor geographic variations notwithstanding. Results from this study are consistent with such studies, and may be partly explained by China's changing social norms concerning homosexuality, brought about by the rapid economic and social development of the past thirty years. In traditional culture in China, MSM were severely socially marginalized and stigmatized. Virtually all MSM faced strong social pressure to hide their sexual orientation, and most of them eventually married. Today, China's social environment is gradually becoming less

stigmatizing for MSM, whereby younger MSM are more active in homosexuality than older MSM. Older MSM are also more likely to be married. Furthermore, our previous study conducted in the same area showed that younger MSM were more likely to use the internet for sex seeking than older MSM[21], implying that younger MSM were likelier to have more casual sex partners and face higher risk. Meanwhile, these study results also imply that intervention and prevention should be focused on MSM with lower education and multiple male sex partners.

Our study has several limitations. Study subjects were recruited using non-random sampling methods that could have led to selection bias. Although the cohort retention was high, HIV, HSV-2, and syphilis incidence rates may have been significantly different among those lost to follow-up. This may have led to overestimation or underestimation of the true incidence. However, our baseline analyses indicated that demographic and behavioral characteristics were similar between those lost to follow-up and those retained in the cohort.

In conclusion, this cohort study was able to maintain a high retention rate and demonstrate that HIV incidence is extremely high among MSM in Beijing. Such findings indicate that the HIV epidemic among MSM in Beijing is more serious than previously expected and is rapidly intensifying. Given the synergistic relationship

between STD and HIV infection, interventions for high risk behaviors and treatment and management for STDs should be combined with HIV control and prevention initiatives among MSM in China. We believe data from this study will help guide future research towards innovative STD/HIV interventions for MSM in China, and mobilize government, public health and non-governmental communities to control the rapid transmission of HIV and STDs among Chinese MSM. Comprehensive actions are urgently needed and the time is now.

AUTHOR'S CONTRIBUTIONS

Dongliang Li, Shuming Li and Yingjie Liu: study design and data collection, manuscript writing.

Yanjie Gao, Mingrun Yu, Xueying Yang, Qingchun Li, Shulin Jiang, Zhenhai Zhou, Zheng Zhang, Li Yan, Guiyan Jiang, Dong Xiao: study design, data collection and manuscript writing

Stephen W. Pan, Yuhua Ruan, Fengji Luo, Yiming Shao: study design, data collection, data interpretation and manuscript writing.

Qingchun Li and Yuhua Ruan: data analysis.

Fengji Luo, Yiming Shao: PI.

The paper has been reviewed by biostatistician, Lu Yin, PhD., Vanderbilt Institute for Global Health, and Departments of Pediatrics, Biostatistics, and Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37203 USA

The paper has been edited by Stephen W. Pan, The School of Population and Public Health University of British Columbia, Vancouver, BC, Canada

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Table 1. Baseline characteristics of study participants

Factors	N	%
Overall	797	100
Age (median, years)	28	
Ethnicity		
Han	738	92.6
Minority	59	7.4
Education		
Less than high school	383	48.1
High school and above	414	51.9
Beijing permanent resident	149	18.7
Monthly income (median, US $)	294	
Marital status in the past 3 months		
Single	492	61.7
Married	141	17.7
Cohabiting with male or female sex partner	125	15.7
Separated or divorced or widowed	39	4.9
Sexual orientation		
Homosexual	539	67.6
Heterosexual or bisexual	258	32.4
Age of sexual debut (median, years)	20	
Age of homosexual debut (median, years)	25	
Partner of sexual debut		
Male	524	65.8
Female	273	34.2

Number of male sex partners in the past 6 months (median)	2	
Bought or sold sex with male sex partners in the past 6 months	48	6.0
Had unprotected anal sex with regular male sex partners in the past 6 month	189	23.7
Had unprotected anal sex with casual male partners in the past 6 month	103	12.9
Had sex with female sex partners in the past 6 months	141	17.7
Had unprotected sex with female sex partners in the past 6 month	94	11.8
Used illicit drugs in the past 6 months	8	1.0
Had STD syndrome in the past year	137	17.2
Syphilis positive	131	16.4
HSV-2 positive	37	4.6

Table 2. Contact patterns and times for cohort follow-up study

Follow-up	Cell phone call	Short text message	QQ/MSN	Peer contact	Email	Landline Telephone	Total
6-month	884	1075	665	87	31	5	2747
12-month	908	1104	704	93	43	2	2854
Total (%)	1792(32.0)	2179(38.9)	1369(24.4)	180(3.2)	74(1.3)	7(0.1)	5601(100.0)

Table 3. Factors associated with HIV seroconversions in a 12-month follow-up study among MSM

Factors	No. of seroconversions	Person-years	Incidence rate (per 100 person years)	HR (95% CI)	*P* value	*Adjusted* HR (95% CI)	*P* value
Total	48	592.98	8.09				
Age (years)							
>25	24	389.31	6.16	1.00		1.00	
≤25	24	203.67	11.78	1.96 (1.11, 3.45)	0.0198	2.59(1.41,4.75)	0.0021
Ethnicity							
Minorities	2	43.32	4.62	1.00			
Han	46	549.66	8.37	1.79 (0.44, 7.39)	0.4191		
Years of education							
>12	16	317.66	5.04	1.00		1.00	
≤12	32	275.31	11.62	2.68(1.43,5.02)	0.0021	2.12(1.12,4.03)	0.0213
Married/cohabiting with female sex partner							
No	36	401.14	8.97	1.00			
Yes	12	191.84	6.26	0.70 (0.36, 1.34)	0.2822		
Beijing permanent resident							
No	41	481.63	8.51	1.00			
Yes	7	111.34	6.29	0.74 (0.33, 1.64)	0.4542		
Monthly income (US $)							
≤440	32	388.45	8.24	1.00			
>440	16	204.52	7.82	0.94 (0.52, 1.71)	0.8365		
Sexual orientation							
Heterosexual/bisexual	10	194.52		1.00			
Homosexual	38	398.45	9.54	1.84 (0.92, 3.69)	0.0871		

Sought male sex partners on the internet							
No	19	255.49	7.44	1.00			
Yes	29	337.48	8.59	1.16 (0.65, 2.06)	0.6227		
Sought male sex partners in bathhouse/public washroom/park							
No	32	442.51	7.23	1.00			
Yes	16	150.46	10.63	1.48 (0.81, 2.70)	0.1994		
Had HIV test in the past year							
No	23	269.11	8.55	1.00			
Yes	25	323.87	7.72	0.89 (0.50, 1.56)	0.6789		
Participated in an HIV intervention program in the past year							
No	7	92.43	7.57	1.00			
Yes	41	500.55	8.19	1.08 (0.48, 2.40)	0.8555		
Number of MSM social contacts							
≤10	30	348.52	8.61	1.00			
>10	18	244.46	7.36	0.86 (0.48, 1.54)	0.6056		
Number of male sex partners in P6 M							
≤1	9	218.23	4.12	1.00		1.00	
>1	39	374.75	10.41	2.54 (1.23, 5.24)	0.0117	2.52(1.20,5.32)	0.015
Had unprotected anal sex with male in P6 M							
No	30	361.94	8.29	1.00			
Yes	18	231.04	7.79	0.94 (0.52, 1.69)	0.8469		
Had commercial sex with male in P6 M							
No	46	569.25	8.08	1.00			
Yes	2	23.73	8.43	1.06 (0.26, 4.38)	0.9314		
Had female sex partners in P6 M							

No	40	481.90	8.30	1.00			
Yes	8	111.08	7.20	0.87 (0.41, 1.86)	0.7249		
Had unprotected sex with female partners in P6 M							
No	43	520.92	8.25	1.00			
Yes	5	72.06	6.94	0.84 (0.33, 2.13)	0.7152		
Had STD syndrome in P6 M							
No	38	512.54	7.41	1.00			
Yes	10	80.43	12.43	1.69 (0.84, 3.40)	0.1388		
Bought condom/lubricant in P6 M							
No	26	321.90	8.08	1.00			
Yes	22	271.08	8.12	1.00 (0.57, 1.77)	0.9891		
Syphilis positive							
No	34	502.95	6.76	1.00		1.00	
Yes	14	90.02	15.55	2.35(1.26, 4.38)	0.0072	2.28(1.19,4.34)	0.0126
HSV-2 positive							
No	39	533.50	7.31	1.00		1.00	
Yes	9	59.48	15.13	2.07 (1.00, 4.27)	0.0497	4.01(1.61,9.97)	0.0029

P6M: the past 6 months.

Mr. Richard Sands
Managing Editor, BMJ Open

Ref.: Manuscript ID bmjopen-2012-001829
HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

Dear Dr. Richard Sands and Dr. Hongjie Liu,

Many thanks for the revision opportunity. Following your guidance, all of the issues and concerns raised were addressed point-by-point.

You state that: 'The paper has been reviewed and edited by an experienced biostatistician and a scientific medical writer whose mother tongue is English, both of whom are knowledgeable about the international literature in this area.' Please ensure that these people are acknowledged in the acknowledgements section

The biostatistician is now acknowledged in the acknowledgements section by the following: "We are grateful to Lu Yin of the Vanderbilt University School of Medicine for reviewing the study's statistical analyses." Because the scientific medical writer (Stephen W. Pan) is also a co-author of the manuscript, he is not mentioned in the acknowledgements section. These contributions by Dr. Yin and Mr. Pan have been added to the "Author's contributions" section on page 18. (page 18, lines 18).

The manuscript needs to be edited before published.

We have edited the manuscript in accordance to all reviewer and editorial comments.

The objectives of this study were to estimate HIV incidence and to identify sociodemographic and behavioral factors of HIV seroconversion among MSM in Beijing, China. Strengths of the study include (1) a large cohort study of 797 HIV-seronegative MSM, with repeated measures, (2) a high retention rate (87%) in the 12 months of follow-up, and (3) use of biological measures in additional to behavioral measures. Based on my observations, this group is very strong in HIV research among MSM in China. I read carefully both the revised manuscript and authors' responses to the previous reviewers' comments. The authors were very responsive.

I would say that both heterosexual and heroin injection are still the major HIV transmission modes In China, although HIV is spreading among MSM. Thus, change ' homosexual transmission has now become a major mode of HIV transmission.' Into 'the HIV epidemic is spreading among MSM in China'. (P6: line 21)

This sentence has been changed accordingly and now reads: "Hence, the HIV epidemic in China is still on the rise and spreading among MSM." (Page 6, lines 7)

Subjects were followed-up by cell phones, short text messages, and MSN/QQ/others. It would be interesting to see if sexual behaviors differed among subjects followed-up by the three approaches. (page 12: line 11-16).

After examining the descriptive data, we observed that sexual behaviors did not differ by method of follow-up. (Page 12)

Why did the number of person-years differ in estimating HIV, syphilis, and HSV? (Page 12: line 27-42)

The cumulative person-years for HIV were higher than that of syphilis and HSV because baseline enrollment criteria only required that participants were HIV negative, not necessarily HSV-2 or syphilis negative. Hence, at baseline, 16.4% of participants tested positive for syphilis and were not followed up for syphilis, and 4.6% of participants tested positive for HSV-2 and were not followed up for HSV-2. Therefore, a proportion of individuals contributed to HIV person-years, but did not contribute to syphilis or HSV-2 person years. To make this clearer for the reader, we have modified paragraph 4 in the results section, which now reads as follows: "Among the 797 participants who were seronegative for HIV at baseline, 48 HIV seroconversions were observed over 592.98 person-years of observation, resulting in an incidence rate of 8.09 cases per 100 person-years (95%CI: 6.92 to 9.26). Among the 666 participants who were seronegative for syphilis at baseline, 30 syphilis seroconversions were observed over 506.06 person-years of observation, resulting in an incidence rate of 5.92 cases per 100 person-years (95%CI: 5.44 to 6.40). Among the 760 participants who were seronegative for HSV-2 at baseline, 46 HSV-2 seroconversions were observed over 570.61 person-years of observation, resulting in an incidence rate of 8.06 per 100 person-years (95%CI: 7.56 to 8.56)." (page 12, lines 10)

As many readers do not know the BED test, please explain the purpose of the BED capture immunoassay (BED-CEIA).

To explain the purpose of the BED capture immunoassay, the following text has been added after the 3rd sentence of paragraph 1 in the discussion section: "(Essentially, the BED assay calculates anti-HIV IgG relative to total IgG and is based on the principle that the ratio of anti-HIV IgG to total IgG increases with time shortly after HIV infection. This method enables cross-sectional serosurveys to estimate HIV-1 incidence and distinguish recent infections from long-term infections.)"

Explain the reasons (1) why HIV incidence among MSM in Beijing were higher than it was in other parts of China and (2) HIV incidence in recent years was higher than previous years. (page 13: line 36-54)

To explain the high and steady rise of HIV incidence in Beijing, the following text has been added as the 8th sentence in paragraph 1 of the discussion section: "Explanations for the exceptionally high and steady rise in HIV incidence among Beijing MSM are not entirely clear, but one possibility may be that Beijing's relatively vibrant MSM culture facilitates greater dissasortative sexual mixing between MSM groups, which in turn can increase HIV background prevalence." (Pages 14, lines 1)

After the part of limitation, please summarize your findings and state implication of your findings in terms of HIV intervention for MSM.

The following summary paragraph was added after the limitations section: "In conclusion, this cohort study was able to maintain a high retention rate and demonstrate that HIV incidence is extremely high among MSM in Beijing. Such findings indicate that the HIV epidemic among MSM in Beijing is more serious than previously expected and is rapidly intensifying. Given the synergistic relationship between STD and HIV infection, interventions for high risk behaviors and treatment and management for STDs should be combined with HIV control and prevention initiatives among MSM in China. We believe data from this study will help guide future research towards innovative STD/HIV interventions for MSM in China, and mobilize government, public health and non-governmental communities to control the rapid transmission of HIV and STDs among Chinese MSM. Comprehensive actions are urgently needed and the time is now." (Pages 16-17)

We hope these changes satisfactorily address the reviewers' comments and questions.

Thank you very much!

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Original Article

Title

HIV incidence in a prospective cohort among men who have sex with men in Beijing: Implications for controlling rapid transmission

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Running Head

HIV incidence among MSM in China

Word count of text

2294

Acknowledgements

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Conflicts of Interest: No.

IRB: The study was approved by the institutional review board (IRB) of the National Center for AIDS/STD Control and Prevention of the China CDC.

Data sharing: Supplementary data is available by contacting Dongliang Li, ldl66@126.com

Article Focus:

- In China, homosexual transmission has now become a major mode of HIV transmission. However, HIV incidence among Chinese MSM remains poorly understood.
- To date, findings from the sparse handful of Chinese MSM cohort studies have been limited by small sample sizes, short term follow-up, or heavy loss to follow-up.

Key Messages:

- The present cohort study was conducted to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up.
- This study provides empirical HIV seroincidence data relevant for HIV prevention and intervention planning strategies among MSM in China.

Strengths and Limitations:

- Evidence-based studies among Chinese MSM are urgently needed to provide scientific decisions for prevention and control of HIV transmission.

Abstract

Objectives: 1) To assess the HIV incidence rate among men who have sex with men (MSM) in a large cohort study in Beijing, China; 2) To identify sociodemographic and behavioral risk factors of HIV seroconversion among MSM in Beijing, China.

Design: A prospective cohort study.

Setting: Baseline and follow-up visits were conducted among MSM in Beijing, China.

Participants: A cohort of 797 HIV-seronegative MSM was recruited from August to December 2009, with follow-up occurring after 6 and 12 months.

Primary and secondary outcome measures: At baseline and follow-up visits, participants reported sociodemographic and sexual behavior information, and were tested for HIV, HSV-2, and syphilis with whole blood specimens. Cox regression analysis was used to identify factors associated with HIV seroconversion.

Results: Most study participants (86.8%) were retained by the 12-month follow-up. The HIV, HSV-2 and syphilis incidence rates were 8.09 (95%CI: 6.92 to 9.26), 5.92 (95%CI: 5.44 to 6.40) and 8.06 (95%CI: 7.56 to 8.56) cases per 100 person-years, respectively. HIV seroconversion was significantly associated with being ≤25 years old, having < 12 years of education, having >1 male sex partner in the past 6 months, and being syphilis positive or HSV-2 positive.

Conclusions: The HIV incidence among MSM in Beijing is serious. Interventions and treatment of sexually transmitted diseases (STD) should be combined with HIV control and prevention measures among MSM.

Key Words: HIV; HSV-2; syphilis; men who have sex with men; cohort

BACKGROUND

It is estimated that 780,000 persons were living with HIV/AIDS (PLWHA) in China by the end of 2011, and that homosexual transmission is accounting for a greater proportion of HIV infections. Men who have sex with men (MSM) as a proportion of PLWHA in China rose from 7.3% in 2005, to 11.0% in 2007, and 17.4% in 2011[1]. Of China's 48,000 new HIV infections in 2011, 29.4% were attributed to homosexual transmission[1]. Hence, the HIV epidemic in China is still on the rise and spreading among MSM.

Although many cross-sectional studies have reported on HIV prevalence among MSM in China, data on HIV incidence rates among this sub-population remain limited. Among the only three MSM cohort studies which have been conducted thus far in China, HIV incidence rates ranged between 2.6 and 5.4 cases per 100 person-years[2–4]. Unfortunately, two of these studies were characterized by small sample sizes, short term follow-up, or heavy loss to follow-up. The most recent cohort study was only able to recruit 218 eligible MSM participants, 44% of whom were lost to follow-up[4]. In response, the present cohort study was designed to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up. In order to better guide HIV prevention and intervention programs among MSM in China, this study focuses on two key objectives: 1) Assess the HIV, HSV-2 and syphilis incidence rates among MSM in Beijing, China; and 2) Identify

sociodemographic and behavioral risk factors of HIV seroconversion among MSM in Beijing, China.

METHODS

Study design and participant recruitment

This prospective cohort study was conducted in Beijing, the capital of China. Participants were recruited using three methods. First, study participants were recruited directly through website advertisements by a non-governmental AIDS volunteer group (www.hivolunt.net). Second, peer recruiters were hired and trained to distribute flyers with study related information at MSM-frequented venues (e.g., MSM clubs, bars, parks and bathhouses). Third, study participants were encouraged to refer their peers to enroll in the study. Prospective study participants then came to a Beijing study clinic that was easily accessible via various transportation routes. Baseline participant inclusion criteria included ≥18 years old, male, had anal or oral sex with another male in the past 6 months, and provided written informed consent with their actual name or nickname. Baseline participant exclusion criteria were HIV-seropositive status, lack of contact information, and planned relocation away from Beijing within the next year. A total of 962 participants were screened during administration of the baseline survey from August to December 2009, of whom 61 were HIV positive, 36 could not provide contact information, 56 planned to relocate away from Beijing within the next year, and 12 refused to participate in follow-up

visits; thus, a total of 797 eligible participants were enrolled into the cohort study, each of whom was assigned a unique and confidential study identification code.

Study participants were followed-up for one year, with follow-up visits occurring at 6 and 12 months. At each study visit (i.e., baseline, 6-month follow-up, and 12-month follow-up), trained health professionals conducted one-on-one questionnaire-based interviews with eligible participants in a private room of the study clinic. After interviews were completed, confidential HIV voluntary counseling and testing (VCT) was conducted, followed by a clinical STD examination by experienced physicians. Venipuncture blood samples were collected from each participant and tested for HIV, syphilis and HSV-2. To ensure confidentiality, each participant was required to provide their pre-assigned identification code in order to receive their test results, which became available after one week. All participants who tested positive for HSV-2 and syphilis were referred to an STD clinic or hospital for appropriate treatment. After each completed study visit, participants received 50 RMB (approximately $7.40 USD), 12 free condoms and one free lubricant. At completion of the baseline and 6-month follow-up visits, each participant was asked to return for a follow-up evaluation after 6 months. The study was approved by the Institutional Review Boards of the National Center for AIDS/STD Control and Prevention of the China Center for Disease Control and Prevention.

Questionnaire measures

Sociodemographic measures included participant age, ethnicity, education, marital status, Beijing permanent residency status, income, and housing status. Behavioral measures included self-identified sexual orientation, sought male sex partners on the internet, sought male sex partners in bathhouse/public washroom/park, had HIV tested in the past year, participated in HIV intervention program in the past year, number of MSM social contacts, number of male sex partners in the past 6 months, had commercial sex (i.e., bought or sold sex) with male partners in the past 6 months, had unprotected anal sex with regular or casual male partners in the past 6 months, had sex with female partners in the past 6 months, had STD syndrome in the past 6 months, bought condom/lubricant in the past 6 months, and used illicit drugs in past 6 months.

Laboratory tests

Blood samples were tested for HIV, HSV-2 and syphilis infections. The HIV infection status was determined with an enzyme-linked immunosorbent assay (ELISA) (InTec Products Company, China) screening and an HIV-1/2 Western Blot confirmation (HIV Blot 2.2 WBTM, Genelabs Diagnostics). HSV-2 infection status was determined using ELISA (Trinity Laboratories, USA). Syphilis infection status was determined with a rapid plasma reagin (RPR) test (Shanghai Rongsheng, China) and

confirmation of positive tests by the Treponema pallidum particle assay (TPPA) test (Fujirebio inc., Japan).

Statistical analysis

Questionnaire-based data and biological testing results were recorded, double checked and compared with EpiData software (EpiData 3.0 for windows; The EpiData Association, Odense, Denmark). After corrections, data were then converted and analyzed using statistical analysis system (SAS 9.1 for windows; SAS Institute Inc, Cary, NC). To identify correlates of time to HIV seroconversion, the Cox regression model was used in univariate and multiple regression analyses. Statistically significant variables in univariate analyses were then entered simultaneously into a multiple Cox regression model. The assumed time of seroconversion was the half-way time point between the participant's last negative HIV test and first positive HIV test. Statistical significance was defined as *P*-value <0.05 (two-tailed).

Results

Baseline characters of the participants

Of the 797 participants, 448 were recruited by peer referral, 173 were recruited by the internet, and 158 were recruited by outreach. The median age was 28 years; 92.6%

belonged to the Han ethnic group; and 51.9% graduated from high school or above. Beijing permanent residents accounted for 18.7%; the median monthly income was US $294; 61.7% were single, 17.7% were married, and 15.7% were cohabiting with male or female sex partners; 67.6% identified as homosexual, and 32.4% identified as heterosexual or bisexual. The median age of sexual debut was 20 years old and the median age of homosexual sexual debut was 25 years old; 65.8% and 34.2% experienced their sexual debut with another male and female, respectively.

Regarding behaviors in the past 6 months among study participants, the median number of male sex partners was 2; 6.0% bought or sold sex with male sex partners; 23.7% had unprotected anal sex with regular male sex partners; 12.9% had unprotected anal sex with casual male sex partners; 17.7% had sex with female sex partners; 11.8% had unprotected sex with female sex partners; and 1.0% used illicit drugs. Experience of an STD syndrome in the past year was reported by 17.2% of participants. Baseline prevalence of syphilis and HSV-2 was 16.4% and 4.6%, respectively. Descriptive results are shown in Table 1.

Cohort retention and contact information

Of the 797 participants, 96.5% (769/797) were retained in the cohort at the 6-month follow-up, and 86.8% (692/797) were retained at the 12-month follow-up. Participants

were contacted for their 6 and 12 month follow-up visits by cell phone calls (1792), short text messages (2179) and QQ© (Tencent Inc. Beijing, China) or MSN© online social networking software (1369) (Web Messenger, Microsoft Cooperation, USA) (Table 2). Of the 692 participants retained in the cohort at the 12 month, 393 were followed up by cell phone calls, 121 by short text messages, 136 by QQ/MSN social networking software, and 29 by peer contacts. There was no difference of sexual behaviors among subjects by method of follow-up.

Incidence of HIV, syphilis and HSV-2 and factors predicting HIV seroconversion

Among the 797 participants who were seronegative for HIV at baseline, 48 HIV seroconversions were observed over 592.98 person-years of observation, resulting in an incidence rate of 8.09 cases per 100 person-years (95%CI: 6.92 to 9.26). Among the 666 participants who were seronegative for syphilis at baseline, 30 syphilis seroconversions were observed over 506.06 person-years of observation, resulting in an incidence rate of 5.92 cases per 100 person-years (95%CI: 5.44 to 6.40). Among the 760 participants who were seronegative for HSV-2 at baseline, 46 HSV-2 seroconversions were observed over 570.61 person-years of observation, resulting in an incidence rate of 8.06 per 100 person-years (95%CI: 7.56 to 8.56).

Univariate and multivariate Cox regression analyses indicated that younger age, less education, having multiple male sex partners in the past 6 months, syphilis infection and HSV-2 infection were significantly associated with time to HIV seroconversion (table 3). Results of the univariate and multivariate Cox regression analyses are shown in Table 3.

Discussion

The first objective of this large cohort study was to assess the HIV incidence rate among MSM in Beijing, China. Results indicate that the HIV incidence rate among MSM has increased dramatically. Using the BED capture immunoassay (BED-CEIA), previous cross-sectional studies among MSM in Beijing have estimated HIV incidence at 2.9% in 2005 and 3.6% in 2006[5]. (Essentially, the BED assay calculates anti-HIV IgG relative to total IgG and is based on the principle that the ratio of anti-HIV IgG to total IgG increases with time shortly after HIV infection. This method enables cross-sectional serosurveys to estimate HIV-1 incidence and distinguish recent infections from long-term infections.) Previous prospective cohort studies conducted among MSM in Beijing found that the incidence rate increased from 2.6 cases per 100 person-years in 2007 to 3.4 cases per 100 person-years in 2008[2,6]. However, our large cohort study conducted from 2009-2010 shows that the HIV incidence rate among Beijing MSM has now increased to 8.09 cases per 100 person-years, an extremely high rate compared with other cities in both China and

around the world[2–4,7–9]. Explanations for the exceptionally high and steady rise in HIV incidence among Beijing MSM are not entirely clear, but one possibility may be that Beijing's relatively vibrant MSM culture facilitates greater dissasortative sexual mixing between MSM groups, which in turn can increase HIV background prevalence. Previous cross-sectional studies conducted among MSM in Beijing showed increasing HIV prevalence among this population, from 0.4% in 2004, 4.6% in 2005, to 5.8% in 2006[10], and 6.3% in 2009. The high HIV incidence rate and prevalence among MSM in Beijing indicate that the epidemic in this group is extremely serious and that effective intervention services are urgently needed.

Due to prevailing social stigma against MSM and MSM-associated behaviors in China and worldwide, conventional recruitment and cohort follow-up approaches with MSM remains challenging. Using multiple methods of recruitment and follow-up contact, we were able to retain 86.8% of all 797 participants after 12 months. This is the first large cohort study in China to evaluate the retention rate for a prospective cohort of MSM. Based on previous cohort studies among injection drug users and MSM [11–15], the following protocols were implemented in order to ensure greater participant retention: 1. An explicit cohort retention plan was written and adhered to throughout the study; 2. Peer MSM staff were hired to contact participants; 3. All participants were asked to provide at least two different means of contact; and 4. Participants had the flexibility of choosing cell phone calls, short text messages,

and/or QQ/MSN internet social networking platforms as the means by which study staff contacted them.

Many epidemiological studies have found that HIV infection is strongly associated with HSV-2 and syphilis [16]. In this study, we found that HSV-2 incidence was high among MSM and that HSV-2 infection also increased the risk of HIV acquisition. It has been reported that persistence of HIV-1 receptor-positive cells after HSV-2 reactivation is a potential mechanism for increased risk of HIV-1 acquisition[17]. However, HSV-2 based HIV intervention studies continue to be disappointing, and the mechanisms of association between HSV-2 and HIV infection requires further study[18].

International studies have shown that younger MSM are at higher risk of HIV infection[9,19,20], minor geographic variations notwithstanding. Results from this study are consistent with such studies, and may be partly explained by China's changing social norms concerning homosexuality, brought about by the rapid economic and social development of the past thirty years. In traditional culture in China, MSM were severely socially marginalized and stigmatized. Virtually all MSM faced strong social pressure to hide their sexual orientation, and most of them eventually married. Today, China's social environment is gradually becoming less

stigmatizing for MSM, whereby younger MSM are more active in homosexuality than older MSM. Older MSM are also more likely to be married. Furthermore, our previous study conducted in the same area showed that younger MSM were more likely to use the internet for sex seeking than older MSM[21], implying that younger MSM were likelier to have more casual sex partners and face higher risk. Meanwhile, these study results also imply that intervention and prevention should be focused on MSM with lower education and multiple male sex partners.

Our study has several limitations. Study subjects were recruited using non-random sampling methods that could have led to selection bias. Although the cohort retention was high, HIV, HSV-2, and syphilis incidence rates may have been significantly different among those lost to follow-up. This may have led to overestimation or underestimation of the true incidence. However, our baseline analyses indicated that demographic and behavioral characteristics were similar between those lost to follow-up and those retained in the cohort.

In conclusion, this cohort study was able to maintain a high retention rate and demonstrate that HIV incidence is extremely high among MSM in Beijing. Such findings indicate that the HIV epidemic among MSM in Beijing is more serious than previously expected and is rapidly intensifying. Given the synergistic relationship

between STD and HIV infection, interventions for high risk behaviors and treatment and management for STDs should be combined with HIV control and prevention initiatives among MSM in China. We believe data from this study will help guide future research towards innovative STD/HIV interventions for MSM in China, and mobilize government, public health and non-governmental communities to control the rapid transmission of HIV and STDs among Chinese MSM. Comprehensive actions are urgently needed and the time is now.

AUTHOR'S CONTRIBUTIONS

Dongliang Li, Shuming Li and Yingjie Liu: study design and data collection, manuscript writing.

Yanjie Gao, Mingrun Yu, Xueying Yang, Qingchun Li, Shulin Jiang, Zhenhai Zhou, Zheng Zhang, Li Yan, Guiyan Jiang, Dong Xiao: study design, data collection and manuscript writing

Stephen W. Pan, Yuhua Ruan, Fengji Luo, Yiming Shao: study design, data collection, data interpretation and manuscript writing.

Qingchun Li and Yuhua Ruan: data analysis.

Fengji Luo, Yiming Shao: PI.

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Table 1. Baseline characteristics of study participants

Factors	N	%
Overall	797	100
Age (median, years)	28	
Ethnicity		
Han	738	92.6
Minority	59	7.4
Education		
Less than high school	383	48.1
High school and above	414	51.9
Beijing permanent resident	149	18.7
Monthly income (median, US $)	294	
Marital status in the past 3 months		
Single	492	61.7
Married	141	17.7
Cohabiting with male or female sex partner	125	15.7
Separated or divorced or widowed	39	4.9
Sexual orientation		
Homosexual	539	67.6
Heterosexual or bisexual	258	32.4
Age of sexual debut (median, years)	20	
Age of homosexual debut (median, years)	25	
Partner of sexual debut		
Male	524	65.8
Female	273	34.2

Number of male sex partners in the past 6 months (median)	2	
Bought or sold sex with male sex partners in the past 6 months	48	6.0
Had unprotected anal sex with regular male sex partners in the past 6 month	189	23.7
Had unprotected anal sex with casual male partners in the past 6 month	103	12.9
Had sex with female sex partners in the past 6 months	141	17.7
Had unprotected sex with female sex partners in the past 6 month	94	11.8
Used illicit drugs in the past 6 months	8	1.0
Had STD syndrome in the past year	137	17.2
Syphilis positive	131	16.4
HSV-2 positive	37	4.6

Table 2. Contact patterns and times for cohort follow-up study

Follow-up	Cell phone call	Short text message	QQ/MSN	Peer contact	Email	Landline Telephone	Total
6-month	884	1075	665	87	31	5	2747
12-month	908	1104	704	93	43	2	2854
Total (%)	1792(32.0)	2179(38.9)	1369(24.4)	180(3.2)	74(1.3)	7(0.1)	5601(100.0)

Table 3. Factors associated with HIV seroconversions in a 12-month follow-up study among MSM

Factors	No. of seroconversions	Person-years	Incidence rate (per 100 person years)	HR (95% CI)	*P* value	*Adjusted* HR (95% CI)	*P* value
Total	48	592.98	8.09				
Age (years)							
>25	24	389.31	6.16	1.00		1.00	
≤25	24	203.67	11.78	1.96 (1.11, 3.45)	0.0198	2.59(1.41,4.75)	0.0021
Ethnicity							
Minorities	2	43.32	4.62	1.00			
Han	46	549.66	8.37	1.79 (0.44, 7.39)	0.4191		
Years of education							
>12	16	317.66	5.04	1.00		1.00	
≤12	32	275.31	11.62	2.68(1.43,5.02)	0.0021	2.12(1.12,4.03)	0.0213
Married/cohabiting with female sex partner							
No	36	401.14	8.97	1.00			
Yes	12	191.84	6.26	0.70 (0.36, 1.34)	0.2822		
Beijing permanent resident							
No	41	481.63	8.51	1.00			
Yes	7	111.34	6.29	0.74 (0.33, 1.64)	0.4542		
Monthly income (US $)							
≤440	32	388.45	8.24	1.00			
>440	16	204.52	7.82	0.94 (0.52, 1.71)	0.8365		
Sexual orientation							
Heterosexual/bisexual	10	194.52		1.00			
Homosexual	38	398.45	9.54	1.84 (0.92, 3.69)	0.0871		

Sought male sex partners on the internet							
No	19	255.49	7.44	1.00			
Yes	29	337.48	8.59	1.16 (0.65, 2.06)	0.6227		
Sought male sex partners in bathhouse/public washroom/park							
No	32	442.51	7.23	1.00			
Yes	16	150.46	10.63	1.48 (0.81, 2.70)	0.1994		
Had HIV test in the past year							
No	23	269.11	8.55	1.00			
Yes	25	323.87	7.72	0.89 (0.50, 1.56)	0.6789		
Participated in an HIV intervention program in the past year							
No	7	92.43	7.57	1.00			
Yes	41	500.55	8.19	1.08 (0.48, 2.40)	0.8555		
Number of MSM social contacts							
≤10	30	348.52	8.61	1.00			
>10	18	244.46	7.36	0.86 (0.48, 1.54)	0.6056		
Number of male sex partners in P6 M							
≤1	9	218.23	4.12	1.00		1.00	
>1	39	374.75	10.41	2.54 (1.23, 5.24)	0.0117	2.52(1.20,5.32)	0.015
Had unprotected anal sex with male in P6 M							
No	30	361.94	8.29	1.00			
Yes	18	231.04	7.79	0.94 (0.52, 1.69)	0.8469		
Had commercial sex with male in P6 M							
No	46	569.25	8.08	1.00			
Yes	2	23.73	8.43	1.06 (0.26, 4.38)	0.9314		
Had female sex partners in P6 M							

No	40	481.90	8.30	1.00			
Yes	8	111.08	7.20	0.87 (0.41, 1.86)	0.7249		
Had unprotected sex with female partners in P6 M							
No	43	520.92	8.25	1.00			
Yes	5	72.06	6.94	0.84 (0.33, 2.13)	0.7152		
Had STD syndrome in P6 M							
No	38	512.54	7.41	1.00			
Yes	10	80.43	12.43	1.69 (0.84, 3.40)	0.1388		
Bought condom/lubricant in P6 M							
No	26	321.90	8.08	1.00			
Yes	22	271.08	8.12	1.00 (0.57, 1.77)	0.9891		
Syphilis positive							
No	34	502.95	6.76	1.00		1.00	
Yes	14	90.02	15.55	2.35(1.26, 4.38)	0.0072	2.28(1.19,4.34)	0.0126
HSV-2 positive							
No	39	533.50	7.31	1.00		1.00	
Yes	9	59.48	15.13	2.07 (1.00, 4.27)	0.0497	4.01(1.61,9.97)	0.0029

P6M: the past 6 months.

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